

REMARKS

Claims 1-20 are pending in the application. Claims 1, 4, 11, 14 and 15 have been amended. Support for the amendments to claim 1 can be found, *e.g.*, page 12, lines 14-19; on page 14, lines 1-27, and Example 2 starting on page 18. Support for the amendments to claims 4, 14 and 15 can be found, *e.g.*, on page 13, lines 11-30. Claims 16-20 have been newly added. Support for claims 16-18 can be found, *e.g.*, on page 14, lines 1-27. Support for claims 19 and 20 can be found, *e.g.*, on page 22, lines 6-28. No new matter has been added.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-10 have been rejected under 35 U.S.C. § 112, first paragraph for lack of written description. The Examiner asserts that the length limitation of claim 1 of up to five nucleotides is not supported in the specification.

Applicants have amended claim 1 to stipulate that the length limitation of the nucleotides added to the primers is one. Support for this amendment can be found, *e.g.*, on page 12, lines 14-19; and Example 2 starting on page 18. Claim 1 now complies with the written description requirement. Therefore, Applicants request that this rejection be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-15 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The claims are rejected for reciting the phrases, "without sequencing," and, "first signals..." as shown on page 3 of the Office Action.

The Examiner asserts that the term, "without sequencing," in claims 1 and 11 renders claims 1-15 indefinite. Applicants have amended claims 1 and 11 to omit this term. Applicants submit that the amendment renders the indefiniteness rejection moot and request that the rejection be withdrawn.

The Examiner also asserts that the term, "first signals suggest that the nucleic acids are of a specific sequence," in claim 1, renders claims 1-10 indefinite. Applicants have amended claim 1 to omit reference to this phrase. Therefore, Applicants request that this rejection be withdrawn.

Rejections under 35 U.S.C. § 102(b)

Claim 11 has been rejected, as being anticipated by Rothberg *et al.* WO 97/15690 published May 1, 1997 ("WO 97/15690"). Applicants traverse for reasons detailed below.

The Examiner states that claim 11 remains rejected in light of WO 97/15690 because the limitations added to claim 1 were not added to claim 11. Applicants have amended claim 11, so that the targeted subsequence can only be extended by one nucleotide. This limitation is not taught by WO 97/15690. Therefore, Applicants request that this rejection be withdrawn.

Rejections under 35 USC 103(a)

Claims 1-10 and 12-15 were rejected for obviousness as being unpatentable over WO 97/15690 in view of WO 99/07896. Applicants traverse for reasons detailed below.

The Examiner asserts that WO 99/07986 teaches phasing primers in which the next possible nucleotides are determined, and that it also teaches that additional 4 base pairs is sufficient for uniquely determining the sequence. Applicants have amended claim 1 to specify that only one base pair can be added. This allows for more efficient determination of the unique identity of a targeted nucleic acid. This limitation is not taught by WO 99/07896. On page 26, lines 1-4 of WO 99/07896, the specification reads:

Moreover, it has been demonstrated that information derived from a GeneCalling™ signal, in combination with information representing an additional 4 bp. (*at minimum*) or, preferably, 8 bp. or, more preferably, 12 or more base pairs, is always sufficient to uniquely determine the sequence generating a GeneCalling™ sequence of interest. (Emphasis added).

Thus, WO 99/07896 teaches away from this limitation.

Further, the invention of the instant application gives unexpected results not taught by WO 99/07896. In WO 99/07896, a sequence of at least 4 nucleotides was added to the "poisoning" primer to distinguish one sequence from other sequences. The present specification discusses the shortcomings of the methodology disclosed WO 99/07986. On page 13, lines 24-30, of the specification, applicants note that:

In a successful oligo-competition, all peaks are recapitulated in both traces except for the peak for which the oligo-competition primer was designed. When the GeneCall of a QEA peak are inaccurate, the primer designed is specific to a gene different from that

which is contained in the peak. Therefore, in an unsuccessful oligo-competition reaction, both the oligo-competed and non-oligo-competed traces are identical.

Using the teachings of WO 99/07896, if the sequence first tested did not match the sequence of the targeted nucleic acid, the practitioner would then have to blindly choose another sequence from the group of nucleic acids from which the targeted nucleic acid was to be identified. If this pool of nucleic acids had many members, this hit or miss approach could take many iterations to find the identity of the targeted nucleic acid. In the present invention, since one nucleotide is tested at a time, generally fewer iterations will be necessary in the case of identifying a targeted nucleic acid from a group of many potential identities. As applicants state on page 14, lines 21-27, the disclosed method has a high degree of reliability while lacking shortcomings of the method described in WO 99/07986:

In the present discussion, operation of the method for two cycles at each of the J and R sites of the fragment targeted by the oligo-competing primers provides the identity of four additional nucleotides (the 2 nucleotides 3' of the J restriction enzymes site, and the 2 nucleotides 3' of the R restriction site). Accordingly, the ambiguity in identifying a fragment as originating from a given gene GeneCall™ list for each peak is refined by a factor of 4^4 , or 256, leading to a nearly unique subsequence-length combination, permitting essentially unambiguous gene identification of the restriction fragment.

In view of the above, Applicants respectfully submit that the present invention is not obvious in view of the combined teachings of the cited references. Also, the present invention has unexpected properties not taught in the WO 99/07896 reference. Therefore, Applicants request that this rejection be withdrawn.

Applicants: Bader et al.
U.S.S.N. 09/755,898

CONCLUSION

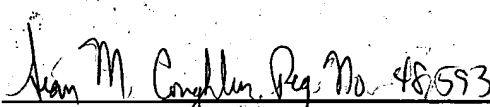
Applicants submit that the application is in condition for allowance and such action is respectfully requested. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

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Respectfully submitted,

TECH CENTER 1600/2900


Ivor R. Elrifi, Reg. No. 39,529
Attorney for Applicants
c/o MINTZ, LEVIN
Tel: (617) 542-6000
Fax: (617) 542-2241
Customer No. 30623

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